ProfhEX
AI-driven platform enabling drug repurposing by in-silico polypharmacology estimations

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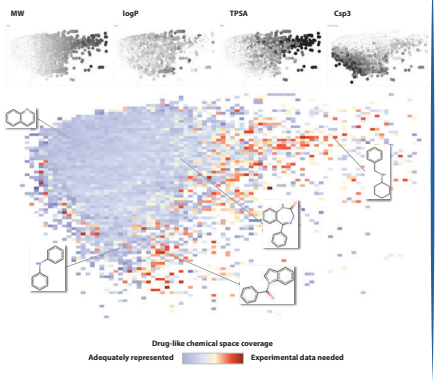
Repurposing is a viable strategy for uncovering novel indications for already approved drugs, as they have the potential to synergistically interact with multiple targets. However, assessing a drug's pleiotropic effect is strongly limited by the scarcity of experimental evidence on drug-target interactions. In-silico simulations play an important role in supplementing missing experimental annotations: ProfhEX is a suite of AI-driven models capable of estimating potential interactions between drugs and therapeutically relevant targets, thereby proposing new drug repurposing strategies.

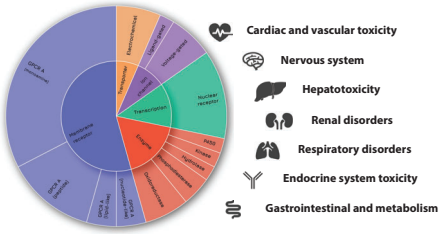
Platform

A first version of ProfhEX focusing on safety profiling has already been published [1], featuring >250K activity data over 46 targets. Models have been generated within the SASviya environment, leveraging state-of-the-art machine learning algorithms, chemistry-aware molecular descriptors "DompeKeys", consensus modelling, applicability domain, uncertainty evaluation and enhanced interpretability.

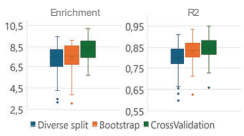
Applicability domain: >85 % of the drug-like chemical space is well-represented by ProfhEX models



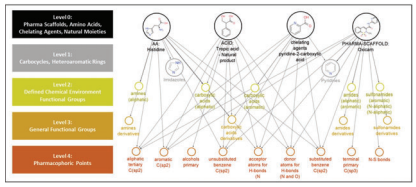
Available models: each ProfhEX model is linked to a specific system organ class (SOC) toxicity, exploiting >1M drug-target side-effects annotations



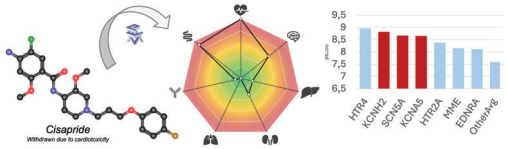
Performance: by coupling a comprehensive validation protocol and the FDA-certified SAS platform, ProfhEX models ensure the highest level of validation and transparency



Encoding: DompeKeys [2] is a novel hierarchical-based descriptor for efficient chemical space mapping, structural moieties interpretation and machine learning

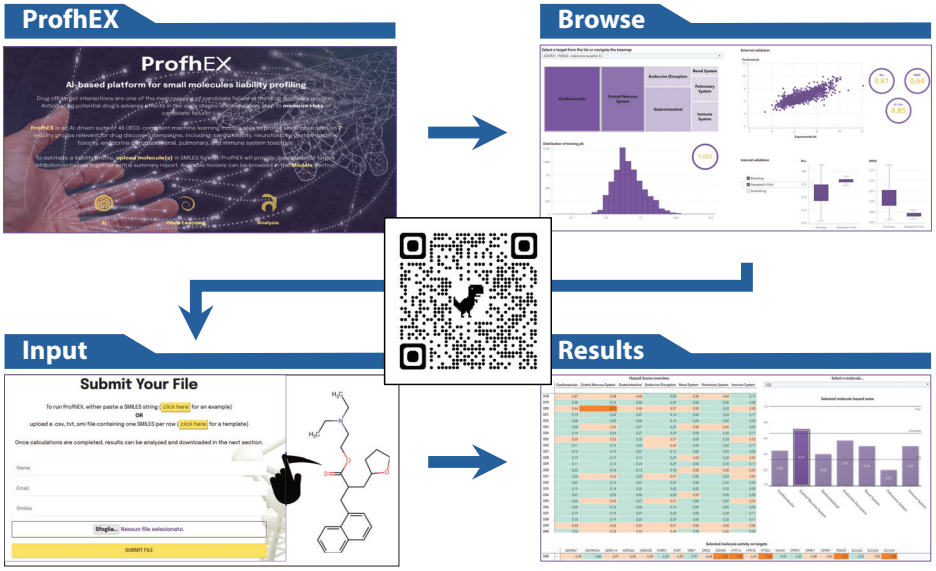


Interpretability: a compound's liability profile is associated to its polypharmacology, providing insights for MoA interpretation



Access

ProfhEX is freely available as webservice enabling high-throughput screening of molecules in a secure, code-free and intuitive cloud environment (https://profhex.exscalate.eu/)



R4ALL Impact

ProfhEX provides estimations for drug-target interactions involving >600 therapeutically relevant targets, offering researchers a freely accessible tool for evaluating new drug repurposing hypotheses. Additionally, the platform can estimate >30 ADME endpoints and identify the most probable metabolic pathways, enabling comprehensive polypharmacological molecule profiling. Therefore, ProfhEX is well-suited to empower R4ALL activities through in-silico driven discovery of new mechanisms of action.

[1] *"ProfhEX: AI-based platform for small molecules liability profiling"*, 10.1186/s13321-023-00728-6, Journal of Cheminformatics
[2] *"DompeKeys": a novel substructure-based descriptor for an efficient chemical space mapping and structural moieties interpretation in Machine Learning models, accepted paper, Journal of Cheminformatics.*